Individualized corrected QT interval improves accuracy to predict mutation carriage in LQTS families compared to Bazett's formula

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INTRODUCTION

Diagnosis in familial long QT syndrome (LQTS) remains challenging due to several difficulties in measuring and interpreting QT interval:

- **QT measurement per se**
- **Variability of QT over time**
- **QT correction for heart rate (HR)**
- **QT overlap**

HYPOTHESIS

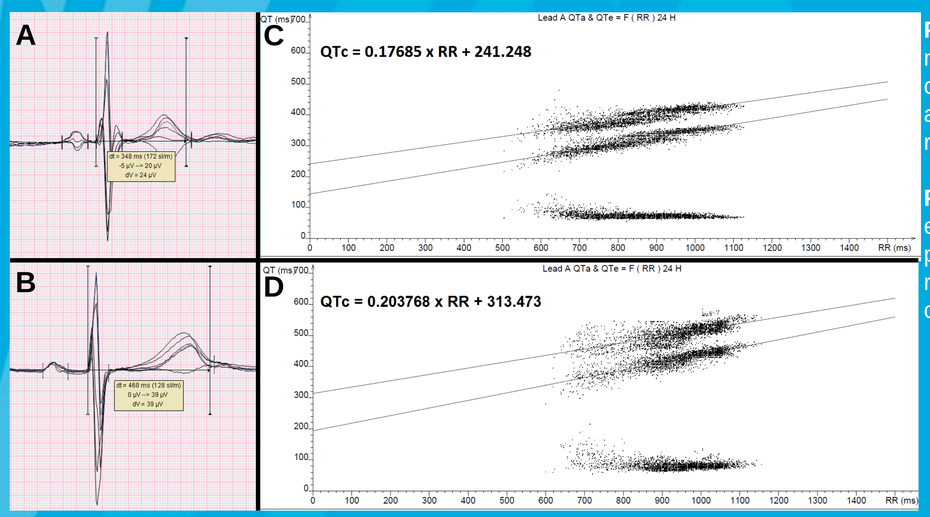
We hypothesized that an individualized corrected QT interval measured by 24 hour holter recording is more accurate in predicting carriage of a pathogenic LQTS mutation compared to standard QT correction with Bazett's formula from standard 12 lead ECG.

The potential advantages of 24 hour holter recordings are:

- **It takes into account QT variability over time,**
- **It uses an individual QT correction formula instead of a generalized formula.**

METHODS

- **Retrospective single center study**
- **Inclusion criteria:**
  - **LQTS patients with known (putative) pathogenic mutation and their genotype negative probands**
  - **Both 24 hour holter recording and standard 12 lead surface ECG available**
  - **To balance the groups addition of concealed AVRT patients after ablation (N=24)**
- **Exclusion criteria:**
  - **Children < 8 years old**
- **ECG measurements (Muse®, GE Healthcare):**
  - **Automated and manual measurements of QT interval and heart rate with high resolution calipers of signal averaged beats of 10 seconds of ECG in lead II and V5; QTend = longest of the 2 measurements; Correction for HR with Bazett's formula (QTc = QT/(RR^(1/2)))**
- **24 hour holter measurements (Synescope™, Ela medical):**
  - **2880 mean complex waveforms (templates), only included if >80% eligible QRS complexes**
  - **Individualized QT correction formula (QTc = α x RR + β)**
  - **α = QT/RR slope = measure of QT heart rate dependence**
  - **QTc = QT at RR = 1000 ms**
- **Statistics: Unpaired t-test, chi square test or 2-way ANOVA for repeated measures were used where appropriate**



Panel A and B: ECG measurement of QTend of a genotype negative and positive subject respectively;

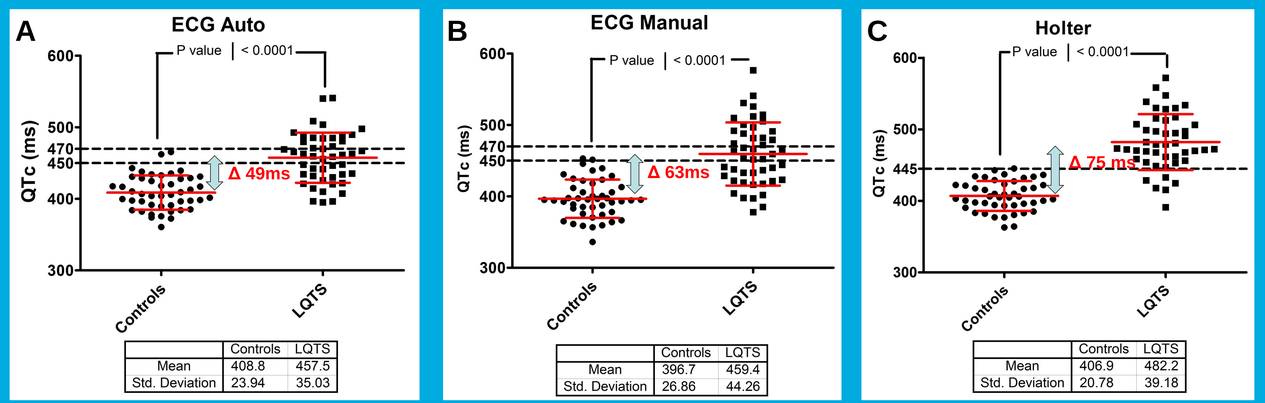
Panel C and D: example of a QT/RR plot with linear regression analysis and corresponding formula

RESULTS

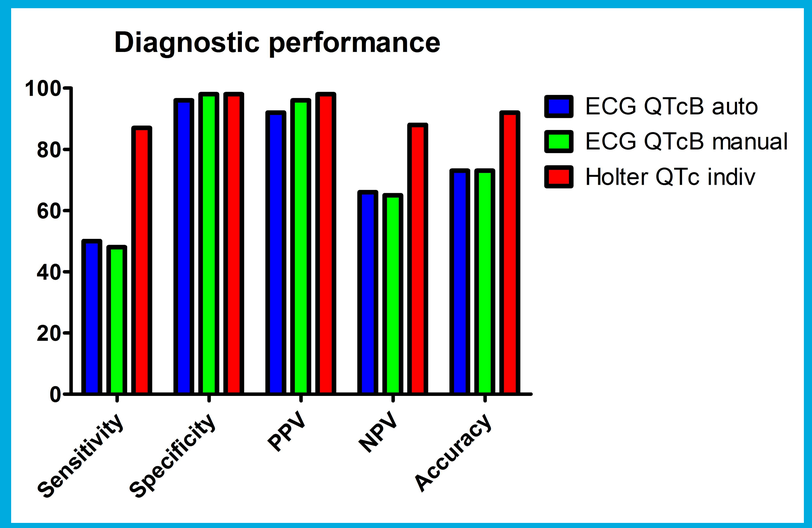
- **Demographic Data**

	Genotype Neg Controls	Genotype Pos LQTS patients	p-value
N	46	46	
Mean Age	35 ± 16	36 ± 16	0.6
Males	27 (59%)	23 (50%)	0.41
Beta blocker therapy	11 (24%)	15 (33%)	0.36
Symptomatic	0	6 (13%)	

- **Difference in QTc between controls and LQTS patients was highly significant increased among the different methods (*p*=0,0002): Automated QTc measured on ECG (Panel A) Vs Vs Manual QTc measured on ECG (Panel B) Vs Individualized QTc measured on 24 hour holter (Panel C). This reduced QTc overlap.**



- **Diagnostic performance of the different techniques**
  - **Conventional cut-off criteria for measurements on ECG (♂<450ms; ♀<470ms)**
  - **Cut-off of 445ms for individualized QTc based on ROC curve of this data set**



CONCLUSION

This study shows for the first time that an individualized QTc measurement derived from holter recordings is superior over QTc measured from a standard 12 lead ECG to predict carriage of a LQTS mutation in LQTS families (diagnostic accuracy 92% vs 73%). Therefore this finding provides evidence for the more widespread use of an individualized QTc in the evaluation of a possible LQTS.